A longitudinal study of the effect of physical activity and cardiorespiratory fitness on insulin and glucose homeostasis in a cohort of children with a family history of obesity

Protocol for PhD work by Mélanie Henderson MD

Quebec Adipose and Lifestyle Investigation in Youth (QUALITY) cohort:

youth with a family history of obesity.

The cohort consists of Caucasian youth, between 8 to 10 years of age at cohort inception, at risk for obesity and its metabolic consequences because of a history of obesity in one or both biological parents.

Exclusion criteria included: a) Child known to have type 1 or type 2 diabetes mellitus; b) Conditions that could interfere with the interpretation of the variables under study, including: treatment with systemic corticosteroids, drugs for hypertension or lipid disorders, severe caloric intake restriction (< 600Kcal/day), chronic disease such as cystic fibrosis, inflammatory bowel disease, renal insufficiency, other; c) Conditions that could limit the child or parents' ability to participate in the study: serious chronic health condition in parent or child, serious cognitive or psychological dysfunction in parents or child.

Recruitment took place over 3 1/2 years. Of the 3350 families who contacted the research team, 1090 families were eligible for the study (33%); of these, 630 families agreed to participate and completed the baseline evaluation (58% of those eligible). The first follow-up visits began in fall 2007, and will be completed in March 2011.

Statistical considerations

Preliminary calculations, assuming perfect measurement of individual changes in PA

The primary objective is to test whether the change in Homa levels is correlated with the change in PA levels. This will be estimated and tested using a multiple linear regression of Homa change on PA change, while accounting for other covariates. So the parameter of interest is the true (theoretical) value of the correlation, R, or equivalently the slope, B, that quantifies this relation.

Because the size of the cohort is already fixed, the calculations here address the precision with which this parameter can be measured by a point estimate r or b, and the ensuing statistical power of the statistical test of the null correlation/slope against various non-null alternatives.

The squared standard error (SE) or precision , i.e., the variance, of a measured slope, b, of n values of y on the corresponding n values of x, can be expressed as $Var[b] = (SD_y)^2 / (n \times \{SD_x\}^2)$. From the general expression linking the components of a test of size alpha (normal deviate Z_α) and power (1-beta) (normal deviate Z_β) of the null H_0: B=0 versus the alternative H_{alt}: $B_{alt} - B_{null} = \Delta_B \neq 0$, to the sample of size n, $Z_\alpha \times SE_{null}[b] + Z_\beta \times SE_{alt}[b] = \Delta_B$
and assuming that the SE is approximately the same under the null and alternative, we can derive the formula in terms of n

$$n = (Z_\alpha + Z_\beta)^2 \times (SD_y)^2 / (\{SD_x\}^2 \times \{\Delta_B\}^2).$$

and use this, with the fixed n, to derive the corresponding power.

If we focus on the correlation R rather than the slope B, the fact that the slope can be wriiten in terms of the correlation, and vice varsa, ie, $B = R \times SD_y / SD_x$, means that the sample size formula simplifies further: $n = (Z_\alpha + Z_\beta)^2 / (\Delta_R)^2$.
[Those interested can verify that this is the formula used in the PS sample size software.]

In our case, with alpha=0.05, so that Z_α=1.96, and beta=0.2, so that Z_β = 0.84, and thus $(Z_\alpha + Z_\beta)$ = 2.8, this simplifies to

$n = 7.84 / (\Delta_R)^2$,

so that the samples size are

784, 196, 87 and 49 for
Δ_R = 0.1, 0.2, 0.3 and 0.4 respectively.

For the sample size we have, namely n=600, the detectable correlation is therefore Δ_R =2.8/sqrt(600) = 0.11.

Correction for attentuation due to (sampling) errors in the measurement of individual changes in PA.

One weeks' measurement of PA initially and again at 2 years will not provide an error free measurement of the true change in a child's PA over 2 years. The detectable Δ_R and the detectable Δ_B are attenuated by the imprecision with which individual changes are measured:

$$\text{detectable } \Delta_R = \Delta_R \,/\, (\text{sqrt}[ICC_x] \times \text{sqrt}[ICC_y]) ;$$

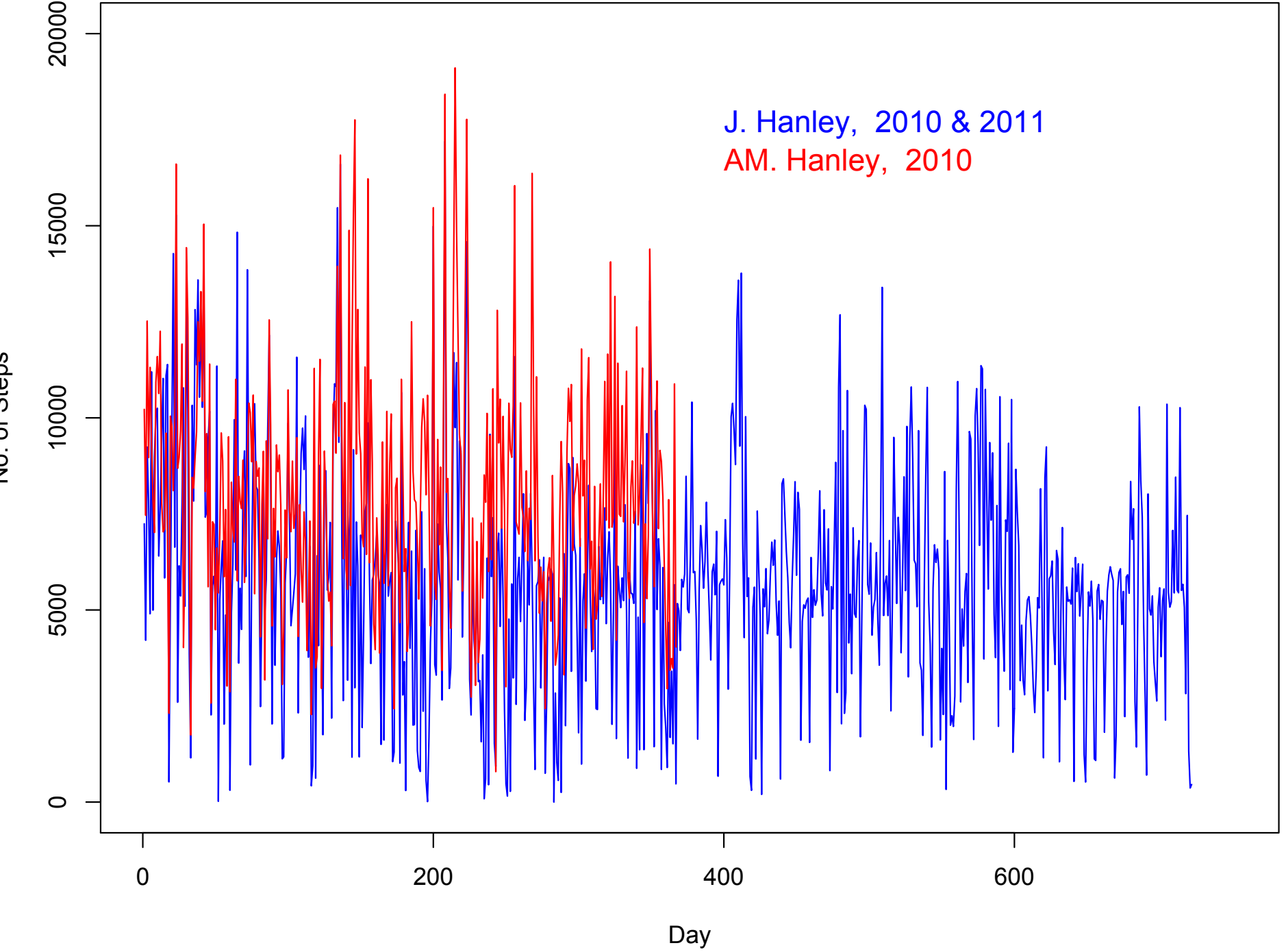
$$\text{detectable } \Delta_B = \Delta_B \,/\, ICC_x \,.$$

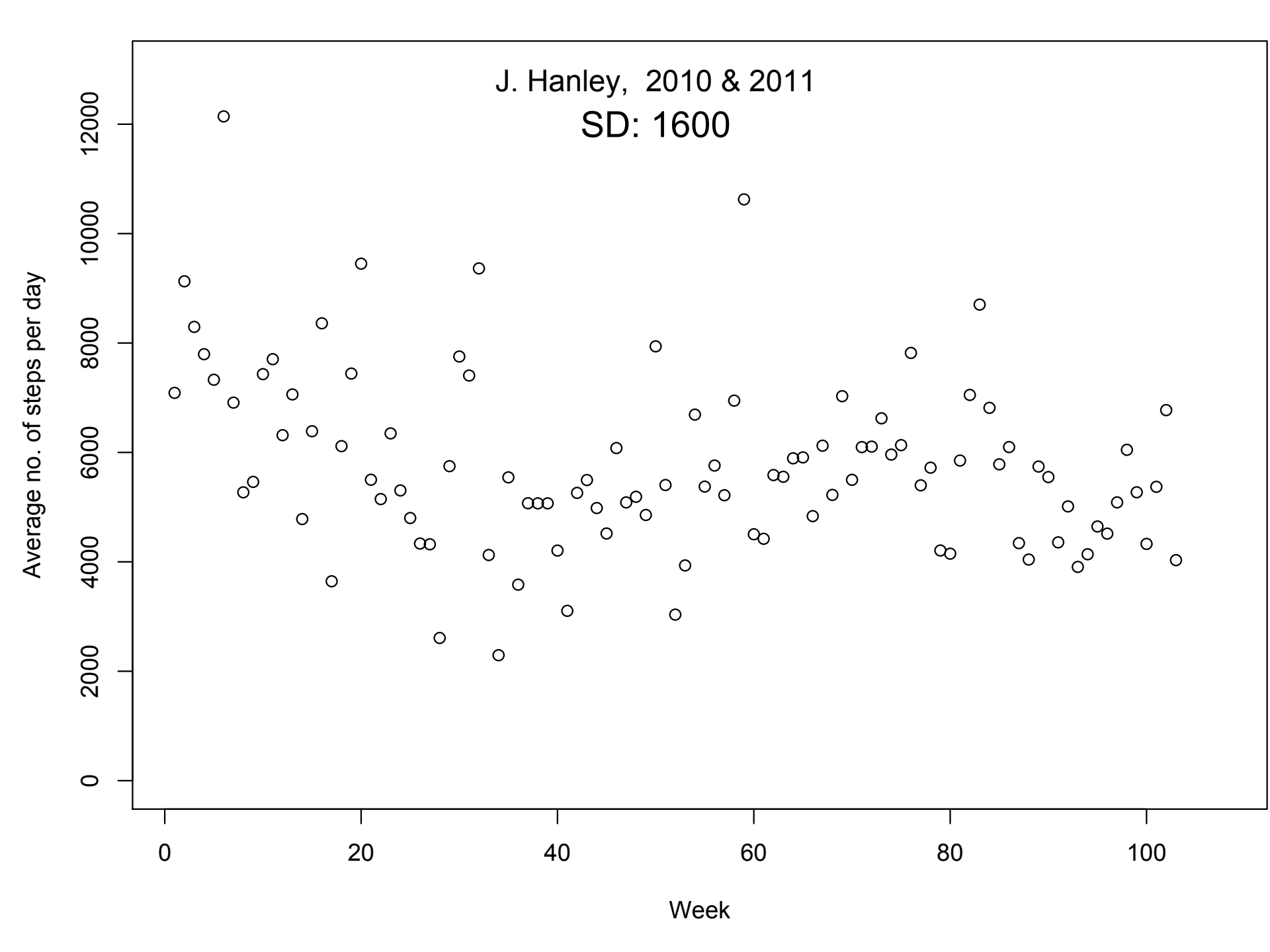
From our analysis of the PA values of 13 children measured for two different weeks 3 months apart, we estimate that the typical coefficient of variation, CV, of the within-child measurements is approx 15%. We assume that the true percentage PA changes will have a between-child SD of 10%. Added to this real between-child variance of $10^2 = 100$ will be an estimated measurement variance of $2 \times 15^2 = 450$ (see note). Thus if the x's of interest in the multiple regression are the observed percentage changes in each child's PA,

$$ICC_x = 100 / (100 + 450) = 0.18.$$

Accordingly, instead of a detectable correlation of 0.11, and assuming a much better ICC of 0.75 for y, the measurement of change in HOMA, we calculate that with our 600 children, the detectable correlation is

detectable Δ_R = $0.11 / (\text{sqrt}[0.18] \times \text{sqrt}[0.75])$ **= 0.3** .


J. Hanley, 2010 & 2011
AM. Hanley, 2010
No. of Steps
0
5000
10000
15000
20000
0
200
400
600
Day


J. Hanley, 2010 & 2011
SD: 1600
Average no. of steps per day
0
2000
4000
6000
8000
10000
12000
0
20
40
60
80
100
Week

Correlations (SEs) between heights of Parents and their Offspring, in family data sent to Francis Galton in 1884

	Father	Mother
Son	0.40 (0.024)	0.30 (0.027)
Daughter	0.36 (0.026)	0.28 (0.028)

K Pearson & A Lee (1902)

errors—for each character is to be noted in the first place. Considering that the measurements are made on more than 4000 individuals of different sexes in more than 1000 families, the conviction is complete that these numbers correspond to a

TABLE IV.

Coefficients of Heredity. Parents and Offspring.

Character	Father and		Mother and	
	Son	Daughter	Son	Daughter
Stature	·514 ± ·015	·510 ± ·013	·494 ± ·016	·507 ± ·014
Span	·454 ± ·016	·454 ± ·014	·457 ± ·016	·452 ± ·015
Forearm	·421 ± ·017	·422 ± ·015	·406 ± ·017	·421 ± ·015

reality in nature. From them we may safely draw the following conclusions for the organs examined:

(*a*) The son and daughter are equally influenced by their father, and equally influenced by their mother.

[Pearson, 1930s] There was thus really quite a well-marked prepotency of the father in the case of stature. Later results on ampler and better material have failed to confirm this prepotency; I think it may well have been due to amateur measuring of stature in women, when high heels and superincumbent chignons were in vogue; it will be noted that the intensity of heredity decreases as more female measurements are introduced. Daughters would be more ready to take off their boots and lower their hair knots, than grave Victorian matrons.

As we have not since succeeded in demonstrating any sex prepotency in parentage, Galton's assumption that such did not exist justifies his theory. But this assumption was not justified by his actual data and affects seriously the values of the constants he reached, which are all too low in the light of more recent research. I think we should be inclined to say now that the regression of the offspring deviates is on the average nearer to 4/5 than to Galton's 2/3 of the midparental deviate.

Galton, however, recognised very fully that his numerical values were only first approximations.

He writes:

"With respect to my numerical estimates, I wish emphatically to say that I offer them only as being serviceably approximate, though they are mutually consistent, and with the desire that they may be reinvestigated by the help of more abundant and much more accurate measurements than those I have at command.

There are many simple and interesting relations to which I am still unable to assign numerical values for lack of adequate material, such as that to which I referred some time back, of the relative influence of the father and the mother on the stature of their sons and daughters.

Data submitted to Galton;
correspondents received either £5 or £7 as prizes, £500 pounds in all

TABLE 9.

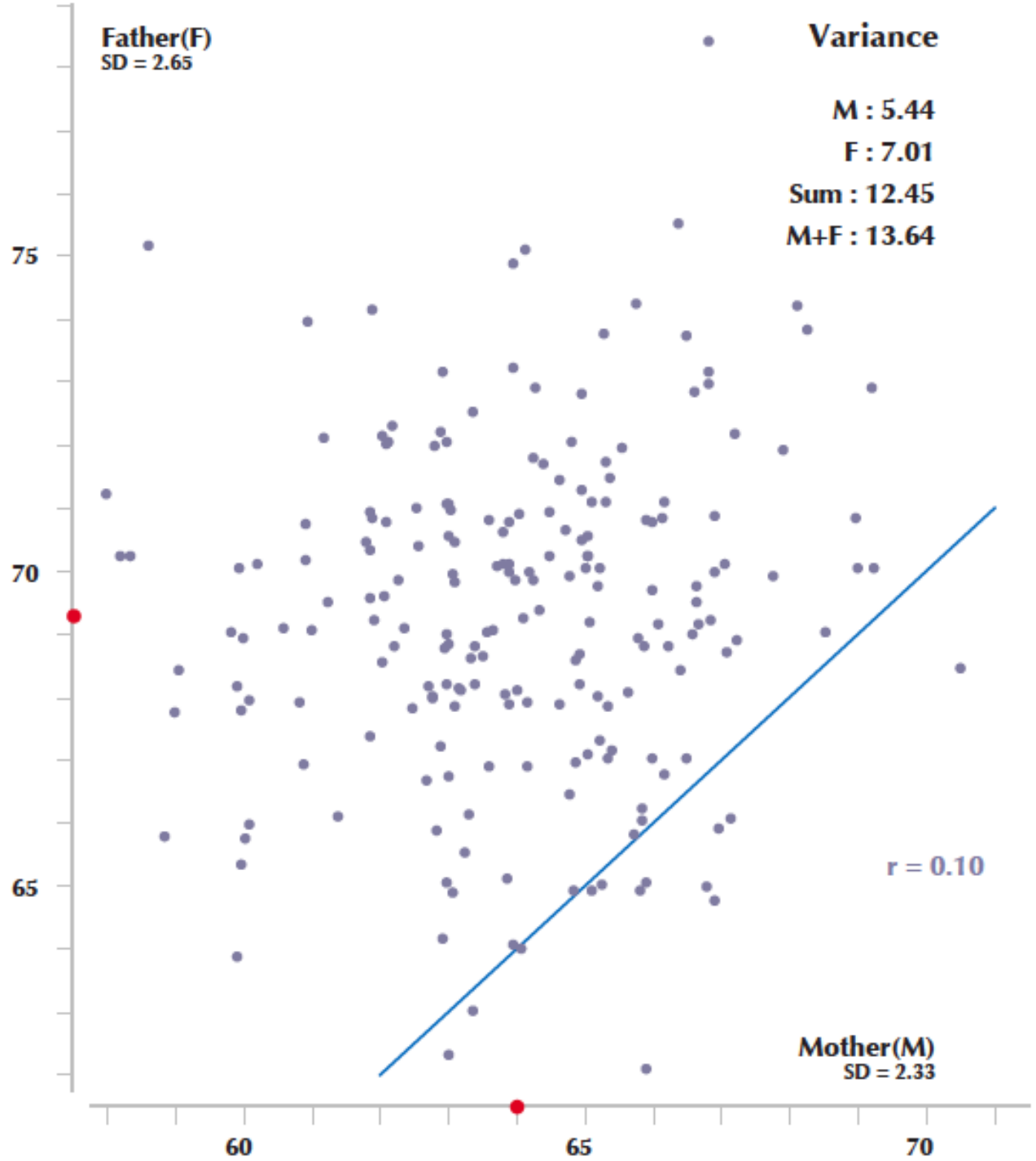
MARRIAGE SELECTION IN RESPECT TO STATURE.

S., t. 12 cases.	M., t. 20 cases.	T., t. 18 cases.
S., m. 25 cases.	M., m. 51 cases.	T., m. 28 cases.
S., s. 9 cases.	M., s. 28 cases.	T., s. 14 cases.

Short and tall, 12 + 14 = 32 cases.
Short and short, 9
Tall and tall, 18 } = 27 cases.

We may therefore regard the married folk as couples picked out of the general population at haphazard when applying the law of probabilities to heredity of stature.

T,M,S = Tall/Medium/Short men; t,m,s = tall/medium/short women.


Father(F)
SD = 2.65
Variance
M : 5.44
F : 7.01
Sum : 12.45
M+F : 13.64
75
70
65
r = 0.10
Mother(M)
SD = 2.33
60
65
70

R =0.10